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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/681,389

10/07/2003

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EXAMINER

POPA, ILEANA

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/681,389	Applicant(s) KENTEN ET AL.	
	Examiner ILEANA POPA	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 December 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 80 and 94-101 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 80 and 94-101 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-79 and 81-93 have been cancelled.

Claims 80 and 94-101 are pending and under examination.

Response to Arguments

Double Patenting

2. The rejection of claims 80 and 94-101 on the ground of nonstatutory obviousness-type double patenting is withdrawn because Applicant submitted a terminal disclaimer on 12/10/2007.

Claim Rejections - 35 USC § 112, 2nd paragraph

3. The rejection of claims 80 and 94-101 under 35 U.S.C. 112, second paragraph, is withdrawn in response to Applicant's arguments filed on 12/10/2007.

Claim Rejections - 35 USC § 112, new matter

4. Claims 89 and 94-101 remain rejected under 35 U.S.C. 112, first paragraph, as introducing new matter, for the reasons of record set forth in the non-final Office action of 09/07/2007. Applicant's arguments filed 12/10/2007 have been fully considered but they are not persuasive.

Applicant traversed the instant rejection on the grounds that the specification as filed and the original claims provide inherent support for claim limitations. Applicant

argues that the original claims as filed in the pending Application recited "...a fusion protein comprising a heat shock protein fused to two or more non-contiguous epitope-containing segments, each epitope containing segment comprising one or more identical or non-identical epitopes..." Applicant submits that if each of the non-contiguous segments contained "one or more identical epitopes" then it is inherent that one of the identical epitopes must be in one of the epitope-containing segments and the other identical epitope must be located in one of the other epitope-containing segments. Thus, Applicant argues, the present language of the pending claims merely clarifies the Applicants' invention as originally filed and claimed and does not, as Examiner stated, add new matter to the specification. Applicant indicates that support for the claims as originally filed may be found in the published application, at paragraph [0023]. For these reasons, Applicant requests the withdrawal of the rejection.

Applicant's arguments are acknowledged, however, the rejection is maintained for the following reasons:

The argument that the present language of the pending claims merely clarifies the Applicants' invention as originally filed and claimed is not found persuasive because the original recitation of "a fusion protein comprising a heat shock protein fused to two or more non-contiguous epitope-containing segments, each epitope-containing segment comprising one or more identical or non-identical epitopes" does not mean that one of the identical epitopes must necessarily be in one of the epitope-containing segment and the other identical epitope must necessarily be in one of the other epitope-containing segment. The original claim language (i.e., each segment) clearly indicates that the

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epitopes are identical within the segment and does not even indicate that the different segments could share epitopes. Applicant points to the specification, paragraph [0023] for support. The indicated paragraph recites:

“A second embodiment of the present invention relates to an ubiquitin fusion protein comprising ubiquitin fused to two or more non-contiguous epitope-containing segments, each epitope-containing segment comprising one or more identical or non-identical epitopes. The non-contiguous locations where fusion is appropriate are internal locations within the ubiquitin moiety, or at the N- or C-terminus of the ubiquitin molecule.”

Again, the recitation of “each epitope-containing segment comprising one or more identical or non-identical epitopes” clearly indicates that the epitopes are identical within segments and not between the segments. For these reasons, the rejection is maintained.

Claim Rejections - 35 USC § 103

5. Claims 80 and 101 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Dalum et al. (J Immunol, 1996, 1545: 4796-4804), in view of both Kierrulf et al. (Mol Immunol, June, 1997, 34: 599-608, Abstract) and Tang et al. (Nature, 1992, 356: 152-154) for the reasons of record set forth in the non-final Office action of 09/07/2007. Applicant's arguments filed 12/10/2007 have been fully considered but they are not persuasive.

Applicant traversed the instant rejection on the grounds that the cited references, alone or in combination, do not teach or suggest synthesis of a DNA vaccine encoding a fusion of a heat shock protein such as ubiquitin with multiple epitopes which would

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result in an immune reaction. Applicant argues that, since none of the references exemplify synthesis of this DNA vaccine, none of the references could possibly teach that such a DNA vaccine would be effective in eliciting an immune response. As such, Applicant argues, one of skill in the art would not be able to deduce from the combined teachings of Dalum, et al., Kjerrulf, et al., and Tang, et al, that a DNA vaccine as recited in claims 80 and 101 would be able to elicit an immune response. Applicant submits that the separate teachings of a heat shock fusion protein, multiple epitopes and using DNA constructs to produce antibodies does not amount to a teaching of the present invention nor give one skilled in the art the motivation or a reasonable expectation of success. In fact, Applicant argues, Tang et al. teach against any reasonable expectation of success when they teach the use of their DNA discoveries and techniques for vaccination as merely "speculative" (p. 154 bridging first and second columns). Applicant argues that, prior to the instant invention, one of skill in the art would not have been able to predict with any degree of certainty that a DNA vaccine encoding a fusion of a heat shock protein with multiple epitopes would result in an immune reaction. Therefore, Applicant requests the withdrawal of the rejection.

Applicant's arguments are acknowledged, however, the rejection is maintained for the following reasons:

Applicant's argument that the cited art does not teach or suggest synthesis of a DNA vaccine encoding a fusion of a heat shock protein such as ubiquitin with multiple epitopes which would result in an immune reaction is just an argument not supported by any evidence. Dalum et al. teach a vaccine comprising a fusion protein between

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ubiquitin and an epitope-containing segment, wherein the vaccine is able to induce an immune response in mice. Although Dalum et al. do not teach their epitope-containing segment as comprising two or more identical epitopes, one of skill in the art would have known to use multiple identical epitopes because the prior art teaches the advantages of using vaccines comprising multiple identical epitopes. For example, Kierrulf et al. teach that incorporating multiple copies of the same epitope enhances the immunogenicity of fusion proteins. Therefore, one of skill in the art would have known and been motivated to enhance immunogenicity by including multiple copies of the same epitope in the vaccine of Dalum et al. Applicant argues that one of skill in the art would not have been able to predict that such a modification would result in a composition able to elicit an immune response. However, Applicant did not provide any evidence that adding more copies of the same immunogenic epitope in the vaccine of Dalum et al. would render their vaccine inoperable. On the contrary, the art teaches that using multiple copies of the same or different epitopes results in more efficient vaccines. Based on the teachings of Kierrulf et al. and on the teachings in the art, one of skill in the art would have had no reason to doubt that such a modification would result in a better immunogenic composition. For these reasons, Applicant's argument is not found persuasive. Similarly, Applicant's argument that Tang et al. teach against any reasonable expectation of success is not found persuasive. The use of "speculative" cannot be equated with a teaching against any reasonable expectation of success. On the contrary, Tang et al. teach that DNA vaccination offers advantages over the use of protein vaccines and suggest its use in the future, as follows:

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"Genetic immunization may be time- and labour-saving in producing antibodies and may offer a unique method of vaccination.

This technique may have at least two useful applications. One is to simplify the procedure and shorten the time required to produce antibodies to particular proteins by eliminating the steps for protein purification and adjuvant administration. The second, more speculative, is the genetic vaccination of animals against pathogenic infections by producing foreign antigens in a restricted subsets of self-cells that mimics natural infection. In this regard, differences in immunological response between genetic and conventional immunization (for example, the duration and magnitude of antibody production or level of T-cell response) may give this protocol useful features."

Therefore, by reading Tang et al., one of skill in the art would not consider them as teaching away from any reasonable expectation of success, especially that their results demonstrate successful immunization with DNA vaccines (see the whole paper by Tang et al.). For these reasons it is concluded that the cited prior art renders the claimed invention *prima facie* obvious and the rejection is maintained.

6. Claims 80, 94-97, 100, and 101 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Dalum et al. taken with Kierrulf et al. and Tang et al., in further view of each Ferro et al. (Eur J Cancer, 1997, 33: 1468-1478, of record), Sacca (Cardiovascular Research, 1997, 36: 3-9, of record), and Johnston et al. (U.S. Patent No. 5,703,057) for the reasons of record set forth in the non-final Office action of 09/07/2007. Applicant's arguments filed 12/10/2007 have been fully considered but they are not persuasive.

Applicant traversed the instant rejection on the grounds that Ferro et al., Sacca, and Johnston et al. do not cure the deficiencies of Dalum et al. taken with Kierrulf et al. and Tang et al.

Applicant's arguments are acknowledged, however, the rejection is maintained for the reasons set forth above.

7. Claims 80, 98, and 101 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Dalum et al. taken with Kierrulf et al. and Tang et al., in further view Hohlfeld (Multiple Sclerosis, 1996, 1: 376-378) for the reasons of record set forth in the non-final Office action of 09/07/2007. Applicant's arguments filed 12/10/2007 have been fully considered but they are not persuasive.

Applicant traversed the instant rejection on the grounds that Hohlfeld does not cure the deficiencies of Dalum et al. taken with Kierrulf et al. and Tang et al.

Applicant's arguments are acknowledged, however, the rejection is maintained for the reasons set forth above.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ileana Popa, PhD

/Joseph T. Woitach/

Supervisory Patent Examiner, Art Unit 1633

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